

## REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **Status of Claims**

Claims 1-15 stand cancelled. Claims 16-29 are pending and currently are under consideration.

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

### **Information Disclosure Statement**

Applicants thank the Examiner for acknowledging the Information Disclosure Statement filed on 11/8/2006.

### **Claims rejections under 35 U.S.C. §112, first paragraph**

The Office maintains the rejection of claims 16-29 under 35 U.S.C. §112, first paragraph as lacking an enabling disclosure. Applicants note the Examiner's clarification that the rejection was for claims 16-29 and not 16-19.

The Office states that:

Affidavits or declarations presented to show that the disclosure of an application is sufficient to one skilled in the art are not acceptable to establish facts which the specification itself should recite. In re Buchner, 929 F. 2d 660, 18 USPQ2d 1331 (Fed. Cir. 1991). Moreover, affidavits or declarations purporting to explain the disclosure or to interpret the disclosure of a pending application are usually not considered. In re Oppenauer, 143 F.2d 974, 62 USPQ 297 (CCPA 1944).

See page 3 of the Office Action.

The Declaration of Dr. Mandel was filed along with an amendment on 20 September 2006 in response to a rejection under 35 U.S.C. §112, first paragraph raised in an Office Action

dated 24 March 2006. Applicants traverse this rejection of the Declaration for the following reasons. The Declaration of Dr. Mandel was not presented to disclose or to interpret the disclosure of the instant application but was rather presented to show that the information that must be read into the specification would have been known to those skilled in the art.

Evidence to supplement a specification which on its face appears deficient under 35 U.S.C. 112 must establish that the information which must be read into the specification to make it complete would have been known to those of ordinary skill in the art. In re Howarth, 654 F.2d 103, 210 USPQ 689 (CCPA 1981)

The Declaration shows that it would have been known to a person of ordinary skill in the art at the time of filing the application that there is a nexus between the administration of apoptotic bodies in the CHS model and the treatment of CHF. The Declaration cites various references that show a connection between decreasing pro-inflammatory cytokines and/or increasing anti-inflammatory cytokines and the treatment of CHF. For example, the Declaration cites various references to show that, firstly<sup>1</sup>, contact hypersensitivity (CHS) is a Th-1 cell-mediated inflammatory disorder involving inflammatory cytokines such as IL-1, TNF- $\alpha$  and IFN- $\gamma$  and that the degree of inflammation associated with CHS is decreased by anti-inflammatory cytokines such as IL-10 (Mandel Declaration at ¶ 4). Secondly, inflammatory cytokines, such as IL-1 $\beta$ , TNF- $\alpha$  and IL-6 play a role in the pathophysiology of congestive heart failure (CHF), characterized by increased circulating levels of these inflammatory cytokines as well as enhanced expression of inflammatory mediators such as TNF- $\alpha$  and IL-6 within the failing myocardium (Mandel Declaration at ¶ 5). Thirdly, IL-10 is able to downregulate pro-inflammatory cytokines such as IL-1 $\beta$  and TNF- $\alpha$  (Mandel Declaration at ¶ 8). Indeed, a decrease in IL-10 levels as well as a decrease in the IL-10 to TNF- $\alpha$  ratio has been correlated with depressed cardiac function in heart failure in rats (Mandel Declaration ¶ 7). Finally, an immunoglobulin-based treatment for patients suffering from CHF, has been shown to increase IL-10 with a slight decrease in TNF- $\alpha$  and IL-1 $\beta$  (Mandel Declaration at ¶ 8).

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<sup>1</sup> Also see Amendment filed 20 September 2006

Therefore, based on the Declaration, one of ordinary skill in the art would require no additional guidance to administer the apoptotic bodies of the invention for the treatment of CHF.

The Office states that the declaration by Dr Mandel fails to show a clear relationship between CHS and CHF and that the declaration is not commensurate in scope to the claimed invention. The Office further states that the claims are drawn to the use of apoptotic bodies in CHF subjects, while the declaration show the administration of anti-inflammatory cytokines. Thus, the declaration is insufficient to overcome the rejection of claims 16-29 based upon the insufficiency of disclosure under 35 U.S.C. §112, first paragraph. *See* pages 3-4 of the Office Action.

Applicants contend that the disclosure of the application, taken along with what is known to those skilled in the art as shown in the Declaration, provides sufficient disclosure to make and use the invention. The Examples of the instant application clearly show the effectiveness of the composition of the invention in preventing and alleviating inflammation due to CHS indicating that the administration of apoptotic cells and bodies of the invention up-regulate the *in vivo* generation of anti-inflammatory Th-2 derived cytokines such as IL-10 and/or down regulates Th-1 inflammatory cytokines such as TNF $\gamma$ , IL-6 and IL-12. *See* page 17, lines 12-18 of the application. Additionally, the Declaration clearly shows it would have been known to a person of ordinary skill in the art at the time of filing the application that there is a nexus between the administration of apoptotic bodies in the CHS model and the treatment of CHF. Therefore, the application provides sufficient guidance to one of skill in the art to make and use the invention.

For the reasons as stated above, withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. Notwithstanding the above and in order to avoid unintended abandonment of this application, Applicants enclose herewith a Notice of Appeal.

### CONCLUSION

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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